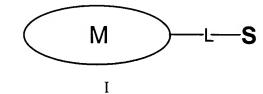
#### **AMENDMENTS TO THE CLAIMS**

1. (Currently Amended) A compound of the formula:



wherein M represents a group of Formula II:

$$H_3C$$
 $y_0$ 
 $y_0$ 

wherein

(i) Z and W independently are >C=O,  $>CH_2$ ,  $>CH-NR_tR_s$ ,  $>N-R_N$  or  $>C=N-R_M$ , wherein

R<sub>t</sub> and R<sub>s</sub> independently are hydrogen or alkyl;

R<sub>M</sub> is hydroxy, alkoxy, substituted alkoxy or OR<sup>p</sup>;

 $R_N$  is hydrogen,  $R^p$ , alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, or - C(X)-NR<sub>t</sub>R<sub>s</sub>; wherein X is =O or =S;

provided that Z and W cannot both simultaneously be, >C=O,  $>CH_2$ ,  $>CH-NR_tR_s$ ,  $>N-R_N$ ,  $>C=N-R_M$  or a bond;

(ii) U and Y independently are hydrogen, halogen, alkyl, or

hydroxyalkyl;

(iii)  $R^1$  is hydroxy,  $OR^p$ ,  $-O-S^2$  group or an =O;

(iv) S<sup>1</sup> is a sugar moiety of Formula III:

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III

wherein

R<sup>8</sup> and R<sup>9</sup> are both hydrogen or together form a bond, or R<sup>9</sup> is hydrogen and R<sup>8</sup> is -N(CH<sub>3</sub>)R<sup>y</sup>, wherein

 $R^y$  is  $R^p$ ,  $R^z$  or  $-C(O)R^z$ , wherein  $R^z$  is hydrogen or alkyl or alkenyl or alkynyl or cycloalkyl or aryl or heteroaryl or alkyl substituted with  $C_2$ - $C_7$ -alkyl,  $C_2$ - $C_7$ -alkenyl,  $C_2$ - $C_7$ -alkynyl, aryl or heteroaryl;

R<sup>10</sup> is hydrogen or R<sup>p</sup>;

S<sup>2</sup> sugar moiety of Formula IV:

wherein

R<sup>3</sup>' is hydrogen or methyl;

 $R^{11}$  is hydrogen,  $R^p$ , or O-R<sup>11</sup> is a group that with  $R^{12}$  and with C/4" carbon atom forms a >C=O or epoxy group;

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R<sup>12</sup> is hydrogen or a group that with O-R<sup>11</sup> group and with C/4" carbon atom forms a >C=O or epoxy group;

- (vi) R<sup>2</sup> is hydrogen, hydroxy, OR<sup>p</sup> or alkoxy;
- (vii) A is hydrogen or methyl;
- (viii) B is methyl or epoxy;
- (ix) E is hydrogen or halogen;

 $R^3$  is hydroxy,  $OR^p$ , alkoxy or  $R^3$  is a group that with  $R^5$  and with C/11 and C/12 carbon atoms forms a cyclic carbonate or carbamate, or if W or Z is >N- $R_N R^3$  is a group that with W or Z forms a cyclic carbamate;

- (xi)  $R^4$  is  $C_1$ - $C_4$  alkyl;
- (xii)  $R^5$  is hydrogen, hydroxy,  $OR^p$ ,  $C_1$ - $C_4$  alkoxy, or a group that with  $R^3$  and with C/11 and C/12 carbon atoms forms a cyclic carbonate or carbamate;
- (xiii) R<sup>6</sup> is hydrogen or C<sub>1</sub>-C<sub>4</sub>-alkyl; and

### R<sup>p</sup> is hydroxyl or amino protective group;

wherein M has a linkage site through which it is linked to S via linking group L; provided that the linkage site being is at one or more of the following:

- a) any reactive hydroxy, nitrogen, or epoxy group located on  $S^1$ ,  $S^2$ , or an aglycone oxygen if  $S^1$  and/or  $S^2$  is cleaved off;
- b) a reactive  $>N-R_N$  or  $-NR_tR_s$  or oxo group located on Z or W;
- c) a reactive hydroxy group located at any one of  $R^1$ ,  $R^2$ ,  $R^3$ , and  $R^5$ ;
- d) any other group that can be first derivatized to a hydroxy or
- -NRtRs group and
- -R<sup>p</sup> is hydroxyl or amino protective group

S represents a group of Formula X:

$$R^{f}$$
 $CH_{3}$ 
 $R^{d}$ 
 $R^{d}$ 
 $R^{d}$ 
 $R^{d}$ 
 $R^{d}$ 
 $R^{d}$ 
 $R^{d}$ 
 $R^{d}$ 
 $R^{d}$ 
 $R^{d}$ 

wherein

R<sup>a</sup> and R<sup>b</sup> independently represents, hydrogen or halogen;

 $R^c$  is hydroxy, alkoxy, alkyl, thiocarbamoyl, carbamoyl or a valence-bond;  $R^d$  and  $R^e$  independently represents: hydrogen, hydroxy, methyl or  $C_1$ - $C_4$ -alkoxy or each are a group that forms a 1,3-dioxolane ring with the other or a valence bond;

R<sup>f</sup> is hydrogen, hydroxy, chloro, or forming a keto group with the carbon atom it is attached to;

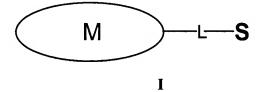
R<sup>j</sup> is hydrogen or halogen;

or a pharmaceutically acceptable salt or solvate thereof;

wherein

L is a linker molecule to which each of M and S are covalently linked.

#### 2. (Currently Amended) A compound of the Formula I:



wherein M represents a group of Formula II:

wherein

(i) Z and W independently are >C=O, >CH<sub>2</sub>, >CH-NR<sub>t</sub>R<sub>s</sub>, >N-R<sub>N</sub> or >C=N-R<sub>M</sub>, wherein

R<sub>t</sub> and R<sub>s</sub> independently are hydrogen or alkyl;

R<sub>M</sub> is hydroxy, alkoxy, substituted alkoxy or OR<sup>p</sup>;

R<sub>N</sub> is hydrogen, R<sup>p</sup>, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, or -

C(X)-NR<sub>t</sub>R<sub>s</sub>; wherein X is =O or =S;

provided that Z and W cannot both simultaneously be, >C=O, >CH<sub>2</sub>, >CH-NR<sub>t</sub>R<sub>s</sub>, >N-R<sub>N</sub>, >C=N-R<sub>M</sub> or a bond;

- (ii) U and Y independently are hydrogen, halogen, alkyl, or hydroxyalkyl;
- (iii) R<sup>1</sup> is hydroxy, OR<sup>p</sup>, -O-S<sup>2</sup> group or an =O;
- (iv)  $S^1$  is a sugar moiety of Formula III:

 $R^8$  and  $R^9$  are both hydrogen or together form a bond, or  $R^9$  is hydrogen and  $R^8$  is  $-N(CH_3)R^y$ , wherein

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 $R^y$  is  $R^p$ ,  $R^z$  or  $-C(O)R^z$ , wherein  $R^z$  is hydrogen or alkyl or alkenyl or alkynyl or cycloalkyl or aryl or heteroaryl or alkyl substituted with  $C_2$ - $C_7$ -alkynyl,  $C_2$ - $C_7$ -alkynyl, aryl or heteroaryl;

R<sup>10</sup> is hydrogen or R<sup>p</sup>;

S<sup>2</sup> sugar moiety of Formula IV:

wherein

R<sup>3</sup>' is hydrogen or methyl;

 $R^{11}$  is hydrogen,  $R^p$ , or O- $R^{11}$  is a group that with  $R^{12}$  and with C/4" carbon atom forms a >C=O or epoxy group;

R<sup>12</sup> is hydrogen or a group that with O-R<sup>11</sup> group and with C/4" carbon atom forms a >C=O or epoxy group;

- (vi) R<sup>2</sup> is hydrogen, hydroxy, OR<sup>p</sup> or alkoxy;
- (vii) A is hydrogen or methyl;
- (viii) B is methyl or epoxy;
- (ix) E is hydrogen or halogen;

 $R^3$  is hydroxy,  $OR^p$ , alkoxy or  $R^3$  is a group that with  $R^5$  and with C/11 and C/12 carbon atoms forms a cyclic carbonate or carbamate, or if W or Z is >N- $R_N \, R^3$  is a group that with W or Z forms a cyclic carbamate;

- (xi)  $R^4$  is  $C_1$ - $C_4$  alkyl;
- (xii) R<sup>5</sup> is hydrogen, hydroxy, OR<sup>p</sup>, C<sub>1</sub>-C<sub>4</sub> alkoxy, or a group that with R<sup>3</sup>

and with C/11 and C/12 carbon atoms forms a cyclic carbonate or carbamate;

(xiii) R<sup>6</sup> is hydrogen or C<sub>1</sub>-C<sub>4</sub>-alkyl; and

R<sup>p</sup> is hydroxyl or amino protective group;

wherein M has a linkage site through which it is linked to S via linking group L; provided that the linkage site being is at one or more of the following:

- a) any reactive hydroxy, nitrogen, or epoxy group located on  $S^1$ ,  $S^2$ , or an aglycone oxygen if  $S^1$  and/or  $S^2$  is cleaved off;
- b) a reactive  $> N-R_N$  or  $-NR_tR_s$  or oxo group located on Z or W;
- c) a reactive hydroxy group located at any one of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>5</sup>;
- d) any other group that can be first derivatized to a hydroxy or
- -NRtRs group; and

R<sup>p</sup> is hydroxyl or amino protective group; and

L represents a group of Formula VA or of Formula VB:

$$X^{1}$$
-(CH<sub>2</sub>)<sub>m</sub>- $X^{2}$ 

$$X^{1}$$
-(CH<sub>2</sub>)<sub>m</sub>-Q-(CH<sub>2</sub>)<sub>n</sub>- $X^{2}$ 

wherein

 $X^{1}$  is selected from: -CH<sub>2</sub>-, -CH<sub>2</sub>NH-, -C(O)-, -OC(O)-, =N-O- or -

OC(O)NH-;

-C(O)NH;

 $X^2$  is -NH- or -NHC(O)- or -CH<sub>2</sub>-;

Q is -NH- or -CH<sub>2</sub>-, wherein

each -CH<sub>2</sub>- or -NH- group may be optionally substituted by C<sub>1</sub>-C<sub>7</sub>-alkyl,

C<sub>2</sub>-C<sub>7</sub>-alkenyl, C<sub>2</sub>-C<sub>7</sub>-alkynyl, C(O)R<sup>x</sup>, C(O)OR<sup>x</sup>, C(O)NHR<sup>x</sup>, wherein R<sup>x</sup> is

 $C_1$ - $C_7$ -alkyl, aryl or heteroaryl;

the symbols m and n independently are a whole number from 0 to 8, with the proviso that if Q is NH, n cannot be 0;

S represents a group of Formula X:

$$R^{i}$$
 $R^{i}$ 
 $R^{i}$ 

wherein

R<sup>a</sup> and R<sup>b</sup> independently represents, hydrogen or halogen;

 $R^c$  is hydroxy, alkoxy, alkyl, thiocarbamoyl, carbamoyl or a valence-bond;  $R^d$  and  $R^e$  independently represents: hydrogen, hydroxy, methyl or  $C_1$ - $C_4$ -alkoxy or each are a group that forms a 1,3-dioxolane ring with the other or a valence bond;

R<sup>f</sup> is hydrogen, hydroxy, chloro, or forming a keto group with the carbon atom it is attached to;

R<sup>j</sup> is hydrogen or halogen; or a pharmaceutically acceptable salt or solvate thereof.

- 3. (Canceled).
- 4. (Canceled)
- 5. (Previously presented) The compound according to claim 2 wherein Z is  $>NR_N$ , wherein  $R_N$  is hydrogen or a methyl group;

W is >CH<sub>2</sub>;

B is methyl;

E is hydrogen;

R<sup>2</sup> is hydroxy;

A is methyl;

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S<sup>1</sup> group represents a group of Formula III wherein

R<sup>8</sup> is selected from: hydrogen, amino, *N*-metylamino, *N*,*N*-dimethylamino,

N-methyl-N-(C<sub>2</sub>-C<sub>4</sub>)-alkylamino, N-methyl-N-methylcarbonylamino,

N-methyl-N-benzylamino, N-methyl-N-cyclohexylamino;

R<sup>9</sup> and R<sup>10</sup> are hydrogen;

 $R^1$  is O-S<sup>2</sup> wherein S<sup>2</sup> represents a group of Formula IV wherein  $R^{11}$  and  $R^{12}$  are hydrogen and  $R^{13}$  is methyl;

U is hydrogen;

Y is methyl;

R<sup>4</sup> is methyl;

R<sup>6</sup> is ethyl;

R<sup>5</sup> is hydroxy or a group that with R<sup>3</sup> and with C/11 and C/12 carbon atoms forms a cyclic carbonate bridge;

R<sup>3</sup> is hydroxy or a group that with R<sup>5</sup> and with C/11 and C/12 carbon atoms forms a cyclic carbonate bridge;

provided that the linkage is through the nitrogen of Z at N/9a position or through the oxygen of  $\mathbb{R}^3$  at C/11 position.

6. (Previously presented) The compound according to claim 2 wherein Z is selected from >N-H, >N-CH<sub>3</sub>, >N-C(O)NHR<sup>x</sup>, wherein R<sup>x</sup> is isopropyl;

W is >C=O or >CH<sub>2</sub> provided that when Z is >N-CH<sub>3</sub> W cannot be >C=O;

B is methyl;

E is hydrogen;

A is methyl;

R<sup>2</sup> is hydroxy or methoxy;

S<sup>1</sup> group represents a group of Formula III wherein

R<sup>8</sup> is selected from: amino, C<sub>1</sub>-C<sub>6</sub>-alkylamino, C<sub>1</sub>-C<sub>6</sub>-dialkylamino;

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R<sup>9</sup> and R<sup>10</sup> are hydrogen;

 $R^1$  is O- $S^2$  wherein  $S^2$  represents a group of Formula IV wherein  $R^{11}$  is hydrogen or

O-R<sup>11</sup> is a group that with R<sup>12</sup> and with C/4"carbon atom forms a >C=O or epoxy group; R<sup>12</sup> is hydrogen or a group that with O-R<sup>11</sup> goup and with C/4"carbon atom forms a >C=O or epoxy group; R<sup>13</sup> is methyl;

U is hydrogen;

Y is methyl;

R<sup>3</sup> is hydroxy;

R<sup>4</sup> is methyl;

R<sup>5</sup> is hydroxy or methoxy;

R<sup>6</sup> is ethyl;

provided that the linkage is through the nitrogen of  $R^8$  at C/3', through the oxygen of  $R^2$  at C/6 or through the carbon of  $R^{12}$  or through the oxygen of  $R^{11}$  both at C/4".

7. (Currently Amended) The compound according to claim 2 wherein R<sup>a</sup> and R<sup>b</sup> independently represents, hydrogen or halogen;

R<sup>d</sup> is hydrogen or hydroxy;

R<sup>e</sup> is methyl;

Rf is hydroxy;

Rj is hydrogen

provided that the linkage is through the valence bond R<sup>k</sup> bond R<sup>C</sup>.

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or a pharmaceutically acceptable salt or solvate thereof.

# 9. (Previously Presented) A compound of the formula

or a pharmaceutically acceptable salt or solvate thereof.

### 11. (Previously Presented) A compound of the formula

or a pharmaceutically acceptable salt or solvate thereof.

### 13. (Previously Presented) A compound of the formula

or a pharmaceutically acceptable salt or solvate thereof.

### 15. (Previously Presented) A compound of the formula

or a pharmaceutically acceptable salt or solvate thereof..

### 17. (Previously Presented) A compound of the formula

or a pharmaceutically acceptable salt or solvate thereof.

### 19. (Previously Presented) A compound of the formula

or a pharmaceutically acceptable salt or solvate thereof.

### 21. (Previously Presented) A compound of the formula

or a pharmaceutically acceptable salt or solvate thereof.

### 23. (Previously Presented) A compound of the formula

or a pharmaceutically acceptable salt or solvate thereof.

# 25. (Previously Presented) A compound of the formula

or a pharmaceutically acceptable salt or solvate thereof.

### 27. (Previously Presented) A compound of the formula

or a pharmaceutically acceptable salt or solvate thereof.

### 29. (Previously Presented) A compound of the formula

or a pharmaceutically acceptable salt or solvate thereof.

### 31. (Previously Presented) A compound of the formula

or a pharmaceutically acceptable salt or solvate thereof.

## 33. (Previously Presented) A compound of the formula

or a pharmaceutically acceptable salt or solvate thereof.

### 35. (Previously Presented) A compound of the formula

or a pharmaceutically acceptable salt or solvate thereof.

#### 37. (Previously Presented) A compound of the formula

or a pharmaceutically acceptable salt or solvate thereof.

### 39. (Previously Presented) A compound of the formula

or a pharmaceutically acceptable salt or solvate thereof.

41. (Previously Presented) A compound of the formula

or a pharmaceutically acceptable salt or solvate thereof.

### 43. (Previously Presented) A compound of the formula

or a pharmaceutically acceptable salt or solvate thereof.

# 45. (Previously Presented) A compound of the formula

or a pharmaceutically acceptable salt or solvate thereof.

# 47. (Previously Presented) A compound of the formula

48. (Currently Amended) A process for the preparation for a compound of Formula I:

wherein M represents a group of Formula II:

wherein

(i) Z and W independently are >C=O,  $>CH_2$ ,  $>CH-NR_tR_s$ ,  $>N-R_N$  or  $>C=N-R_M$ , wherein

R<sub>t</sub> and R<sub>s</sub> independently are hydrogen or alkyl;

R<sub>M</sub> is hydroxy, alkoxy, substituted alkoxy or OR<sup>p</sup>;

R<sub>N</sub> is hydrogen, R<sup>p</sup>, alkyl, alkenyl, alkynyl, alkoxy, alkoxyalkyl, or -C(X)-

 $NR_tR_s$ ; wherein X is =0 or =S;

provided that Z and W cannot both simultaneously be, >C=O, >CH<sub>2</sub>,

>CH-NR<sub>t</sub>R<sub>s</sub>, >N-R<sub>N</sub>, >C=N-R<sub>M</sub> or a bond;

(ii) U and Y independently are hydrogen, halogen, alkyl, or hydroxyalkyl;

- (iii)  $R^1$  is hydroxy,  $OR^p$ ,  $-O-S^2$  group or an =O;
- (iv) S<sup>1</sup> is a sugar moiety of Formula III:

wherein

R<sup>8</sup> and R<sup>9</sup> are both hydrogen or together form a bond, or R<sup>9</sup> is hydrogen and R<sup>8</sup> is -N(CH<sub>3</sub>)R<sup>y</sup>, wherein

 $R^y$  is  $R^p$ ,  $R^z$  or  $-C(O)R^z$ , wherein  $R^z$  is hydrogen or alkyl or alkenyl or alkynyl or cycloalkyl or aryl or heteroaryl or alkyl substituted with  $C_2$ - $C_7$ -alkyl,  $C_2$ - $C_7$ -alkenyl,  $C_2$ - $C_7$ -alkynyl, aryl or heteroaryl;

R<sup>10</sup> is hydrogen or R<sup>p</sup>;

S<sup>2</sup> sugar moiety of Formula **IV**:

wherein

R<sup>3</sup>' is hydrogen or methyl;

 $R^{11}$  is hydrogen,  $R^p$ , or O-R<sup>11</sup> is a group that with  $R^{12}$  and with C/4" carbon atom forms a >C=O or epoxy group;

R<sup>12</sup> is hydrogen or a group that with O-R<sup>11</sup> group and with C/4" carbon atom forms a >C=O or epoxy group;

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- (vi) R<sup>2</sup> is hydrogen, hydroxy, OR<sup>p</sup> or alkoxy;
- (vii) A is hydrogen or methyl;
- (viii) B is methyl or epoxy;
- (ix) E is hydrogen or halogen;

 $R^3$  is hydroxy,  $OR^p$ , alkoxy or  $R^3$  is a group that with  $R^5$  and with C/11 and C/12 carbon atoms forms a cyclic carbonate or carbamate, or if W or Z is >N- $R_N R^3$  is a group that with W or Z forms a cyclic carbamate;

- (xi)  $R^4$  is  $C_1$ - $C_4$  alkyl;
- (xii)  $R^5$  is hydrogen, hydroxy,  $OR^p$ ,  $C_1$ - $C_4$  alkoxy, or a group that with  $R^3$  and with C/11 and C/12 carbon atoms forms a cyclic carbonate or carbamate;
- (xiii) R<sup>6</sup> is hydrogen or C<sub>1</sub>-C<sub>4</sub>-alkyl; and

#### R<sup>p</sup> is hydroxyl or amino protective group;

wherein M has a linkage site through which it is linked to S via linking group L; provided that the linkage site being is at one or more of the following:

- a) any reactive hydroxy, nitrogen, or epoxy group located on  $S^1$ ,  $S^2$ , or an aglycone oxygen if  $S^1$  and/or  $S^2$  is cleaved off;
- b) a reactive  $> N-R_N$  or  $-NR_tR_s$  or oxo group located on Z or W;
- c) a reactive hydroxy group located at any one of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>5</sup>;
- d) any other group that can be first derivatized to a hydroxy or -NR<sub>t</sub>R<sub>s</sub> group; and

R<sup>p</sup> is hydroxyl or amino protective group.

L represents a group of Formula VA or of Formula VB:

$$VA X1-(CH2)m-X2$$

**VB** 
$$X^{1}$$
-(CH<sub>2</sub>)<sub>m</sub>-Q-(CH<sub>2</sub>)<sub>n</sub>- $X^{2}$ 

wherein

 $X^1$  is selected from: -CH<sub>2</sub>-, -CH<sub>2</sub>NH-, -C(O)-, -OC(O)-, =N-O- or -

OC(O)NH-;

-C(O)NH;

 $X^2$  is -NH- or -NHC(O)- or -CH<sub>2</sub>-;

Q is -NH- or -CH<sub>2</sub>-, wherein

each -CH<sub>2</sub>- or -NH- group may be optionally substituted by C<sub>1</sub>-C<sub>7</sub>-alkyl,

C2-C7-alkenyl, C2-C7-alkynyl, C(O)Rx, C(O)ORx, C(O)NHRx, wherein Rx is

 $C_1$ - $C_7$ -alkyl, aryl or heteroaryl;

the symbols m and n independently are a whole number from 0 to 8, with the proviso that if Q is NH, n cannot be 0;

S represents a group of Formula X:

$$R^{f}$$
 $CH_3$ 
 $R^{d}$ 
 $R^{d}$ 
 $R^{d}$ 
 $R^{d}$ 
 $R^{d}$ 
 $R^{d}$ 
 $R^{d}$ 
 $R^{d}$ 

wherein

R<sup>a</sup> and R<sup>b</sup> independently represents, hydrogen or halogen;

 $R^{c}$  is hydroxy, alkoxy, alkyl, thiocarbamoyl, carbamoyl or a valence-bond;

R<sup>d</sup> and R<sup>e</sup> independently represents: hydrogen, hydroxy, methyl or C<sub>1</sub>-C<sub>4</sub>-alkoxy or each are a group that forms a 1,3-dioxolane ring with the other or a valence bond;

R<sup>f</sup> is hydrogen, hydroxy, chloro, or forming a keto group with the carbon atom it is attached to;

R<sup>j</sup> is hydrogen or halogen;

or a pharmaceutically acceptable salt or solvate;

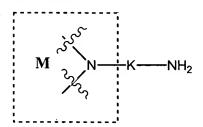
a) for a compound represented by Formula I comprising the steps of:

where X<sup>2</sup> is -NHC(O)-, by reacting a compound of Formula V:



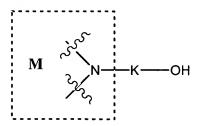
 $\mathbf{v}$ 

wherein L<sup>1</sup> represents a leaving group, and a free amino group of a macrolide represented by Formula VId:



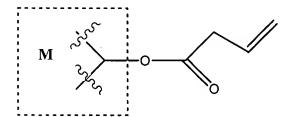
#### **VId**

b) for a compound represented by Formula I, where  $X^2$  is -OC(O)-, by reacting a compound of Formula V and a hydroxyl group of a macrolide represented by Formula VIe:



VIe

c) for a compound represented by Formula I, wherein  $X^1$  is -OC(O)-, Q is NH and  $X^2$  is -NHC(O)-, by reacting a macrolide represented by:



and a free amino group of the compound represented by Formula IVc:

IVc

d) for a compound represented by Formula I, where  $X^1$  is -OC(O)NH- and  $X^2$  is -NHC(O)-, by reacting a macrolide represented by Formula VII and a free amino group of Formula IVc:

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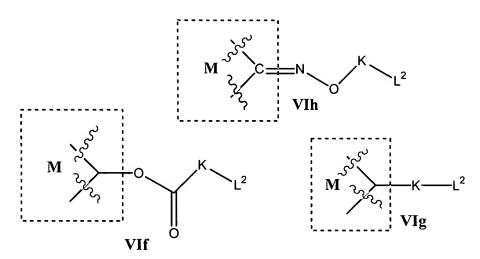
VII

e) for a compound represented by Formula I,  $X^1$  is -CH<sub>2</sub>-, Q is -NH- and  $X^2$  is -NHC(O)-, by reacting a macrolide represented by Formula Va and a compound of Formula V:

Va

f) compound of Formula I by reacting a macrolide represented by Formula VIf or by Formula VIg or by Formula VIh having a leaving group  $L_2$ 

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with a free carboxyl acid of steroid represented by Formula IVb

g) for a compound represented by Formula I, wherein X1 is -OC(O)-, Q is NH and  $X^2$  is -NH- by reacting a macrolide represented by:

$$X^1(CH_2)_mQ(CH_2)_nNH_2$$

#### VId

and a steroid subunit having a -C=C- bond represented by Formula Sb:

following by modification of R<sup>c</sup> group.

Application No.: 10/615,716 39 Docket No.: 03818/100L650-US1

49. (Previously Presented) A pharmaceutical composition comprising a compound according to claim 1 or a pharmaceutically acceptable salt or solvate thereof as well as pharmaceutically acceptable diluent or carrier.

- 50. (Previously Presented) A method of treatment of inflammatory diseases, disorders or conditions characterized by or associated with an undesirable inflammatory immune response, and all diseases and conditions induced by or associated with an excessive secretion of TNF-α and IL-1 which comprises administering to a subject in need of treatment a therapeutically effective amount of a compound according to claim 1.
- 51. (Previously Presented) A method of treating inflammatory conditions or immune or anaphylactic disorders associated with infiltration of leukocytes into inflamed tissue in a subject in need thereof which comprises administering to said subject a therapeutically effective amount of a compound according to claim 1.
- 52. (Previously presented) The method according to claim 51, wherein inflammatory conditions and immune disorders are selected from the group consisting of asthma, adult respiratory distress syndrome, bronchitis, and cystic fibrosis.
- 53. (Previously presented) A method according to claim 51, wherein said inflammatory conditions and immune disorders are selected from the group consisting of inflammatory conditions or immune disorders of the lungs, joints, eyes, bowel, skin, and heart.
- 54. (Previously presented) A method according to claim 51, wherein said inflammatory conditions and immune disorders are selected from the group consisting of asthma, adult respiratory distress syndrome,

bronchitis, cystic fibrosis, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, gouty arthritis, uveitis, conjunctivitis, inflammatory bowel conditions, Crohn's disease, ulcerative colitis, distal proctitis, psoriasis, eczema, dermatitis, coronary infarct damage, chronic inflammation, endotoxin shock, and smooth muscle proliferation disorders.

- 55. (Previously Presented) A pharmaceutical composition comprising a compound according to claim 2, or a pharmaceutically acceptable salt or solvate thereof as well as pharmaceutically acceptable diluent or carrier.
- 56. (Previously Presented) A method of treatment of inflammatory diseases, disorders or conditions characterized by or associated with an undesirable inflammatory immune response, and all diseases and conditions induced by or associated with an excessive secretion of TNF-α and IL-1 which comprises administering to a subject in need of treatment a therapeutically effective amount of a compound according to claim 2.
- 57. (Previously Presented) A method of treating inflammatory conditions or immune or anaphylactic disorders associated with infiltration of leukocytes into inflamed tissue in a subject in need thereof which comprises administering to said subject a therapeutically effective amount of a compound according to claim 2.
- 58. (Previously Presented) The method according to claim 57, wherein inflammatory conditions and immune disorders are selected from the group consisting of asthma, adult respiratory distress syndrome, bronchitis, and cystic fibrosis.
- 59. (Previously Presented) A method according to claim 57, wherein said inflammatory conditions and immune disorders are selected from the

group consisting of inflammatory conditions or immune disorders of the lungs, joints, eyes, bowel, skin, and heart.

- 60. (Previously Presented) A method according to claim 57, wherein said inflammatory conditions and immune disorders are selected from the group consisting of asthma, adult respiratory distress syndrome, bronchitis, cystic fibrosis, rheumatoid arthritis, rheumatoid spondylitis, osteoarthritis, gouty arthritis, uveitis, conjunctivitis, inflammatory bowel conditions, Crohn's disease, ulcerative colitis, distal proctitis, psoriasis, eczema, dermatitis, coronary infarct damage, chronic inflammation, endotoxin shock, and smooth muscle proliferation disorders.
- 61. (New) A compound of the formula:



I

wherein M represents a group of Formula II:

$$H_3C$$
 $y_{a}$ 
 $y_{a}$ 

wherein

(i) Z and W independently are >C=O,  $>CH_2$ ,  $>CH-NR_tR_s$ ,  $>N-R_N$  or  $>C=N-R_M$ , wherein

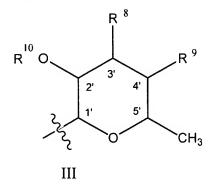
R<sub>t</sub> and R<sub>s</sub> independently are hydrogen or alkyl;

R<sub>M</sub> is hydroxy, alkoxy, or OR<sup>p</sup>;

 $R_N$  is hydrogen,  $R^p$ , alkyl, alkoxy, alkoxyalkyl, or -C(X)-NR<sub>t</sub>R<sub>s</sub>; wherein X is =0 or =S;

provided that Z and W cannot both simultaneously be, >C=O, >CH<sub>2</sub>, >CH-NR<sub>t</sub>R<sub>s</sub>, >N-R<sub>N</sub>, >C=N-R<sub>M</sub> or a bond;

- (ii) U and Y independently are hydrogen, halogen, alkyl, or hydroxyalkyl;
- (iii)  $R^1$  is hydroxy,  $OR^p$ ,  $-O-S^2$  group or an =O;
- (iv)  $S^1$  is a sugar moiety of Formula III:



wherein

R<sup>8</sup> and R<sup>9</sup> are both hydrogen or together form a bond, or R<sup>9</sup> is hydrogen and R<sup>8</sup> is -N(CH<sub>3</sub>)R<sup>y</sup>, wherein

 $R^y$  is  $R^z$  or  $-C(O)R^z$ , wherein  $R^z$  is hydrogen or alkyl or alkenyl or alkynyl or cycloalkyl or aryl or heteroaryl or alkyl substituted with  $C_2$ - $C_7$ -alkyl,  $C_2$ - $C_7$ -alkenyl,  $C_2$ - $C_7$ -alkynyl, aryl or heteroaryl;  $R^{10}$  is hydrogen or  $R^p$ ;

S<sup>2</sup> sugar moiety of Formula IV:

wherein

R<sup>3</sup>' is hydrogen or methyl;

R<sup>11</sup> is hydrogen, or R<sup>p</sup>

R<sup>12</sup> is hydrogen;

(vi) R<sup>2</sup> is hydrogen, hydroxy, OR<sup>p</sup> or alkoxy;

(vii) A is hydrogen or methyl;

(viii) B is methyl or epoxy;

(ix) E is hydrogen or halogen;

 $R^3$  is hydroxy,  $OR^p$ , alkoxy or  $R^3$  is a group that with  $R^5$  forms a cyclic carbonate or carbamate, or if W or Z is  $>N-R_N$   $R^3$  is a group that with W or Z forms a cyclic carbamate;

- (xi)  $R^4$  is  $C_1$ - $C_4$  alkyl;
- (xii)  $R^5$  is hydrogen, hydroxy,  $OR^p$ ,  $C_1$ - $C_4$  alkoxy, or a group that with  $R^3$  forms a cyclic carbonate or carbamate;
- (xiii) R<sup>6</sup> is hydrogen or C<sub>1</sub>-C<sub>4</sub>-alkyl;

R<sup>p</sup> is a protective group

wherein M has a linkage site through which it is linked to S via linking group L; provided that the linkage site being at one or more of the following:

- a) any reactive hydroxy, nitrogen, or epoxy group located on  $S^1$ ,  $S^2$ , or an aglycone oxygen if  $S^1$  and/or  $S^2$  is cleaved off;
- b) a reactive >N-R<sub>N</sub> or -NR<sub>t</sub>R<sub>s</sub> or oxo group located on Z or W;

c) a reactive hydroxy group located at any one of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>5</sup>;

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- d) any other group that can be first derivatized to a hydroxy or
- -NR<sub>t</sub>R<sub>s</sub> group; and

S represents a group of Formula X:

$$R^{f}$$
 $CH_{3}$ 
 $R^{d}$ 
 $R^{d}$ 
 $R^{d}$ 
 $R^{d}$ 
 $R^{d}$ 
 $R^{d}$ 
 $R^{d}$ 
 $R^{d}$ 
 $R^{d}$ 
 $R^{d}$ 

wherein

R<sup>a</sup> and R<sup>b</sup> independently represents, hydrogen or halogen;

R<sup>c</sup> is a valence-bond;

R<sup>d</sup> and R<sup>e</sup> independently represents: hydrogen, hydroxy, methyl or C<sub>1</sub>-C<sub>4</sub>-alkoxy or each are a group that forms a 1,3-dioxolane ring with the other:

R<sup>f</sup> is hydrogen, hydroxy, chloro, or forming a keto group with the carbon atom it is attached to;

R<sup>j</sup> is hydrogen or chloro;

or a pharmaceutically acceptable salt or solvate thereof;

wherein

L is a linker molecule to which each of M and S are covalently linked.

- 62. (New) The compound according to claim 61 wherein
  - (i) Z is  $>N-R_N$  and W is  $>CH_2$ ;
  - (ii)U is H and Y is CH3;
  - (iii) R<sup>1</sup> is an -O-S<sup>2</sup> group;

# (iv) S<sup>1</sup> is a sugar moiety of Formula IIIa:

wherein

R<sup>8</sup> is H or -N(CH<sub>3</sub>)R<sup>y</sup>, wherein

R<sup>y</sup> an alkyl;

S<sup>2</sup> sugar moiety of Formula **IVa**:

- (vi) R<sup>2</sup> is hydroxy;
- (vii) A is CH<sub>3</sub>;
- (viii) B is CH<sub>3</sub>;
- (ix) E is H;
- $(x)R^3$  is OH;
- (xi)  $R^4$  is  $C_1$ - $C_4$  alkyl;
- (xii)  $R^5$  is OH; and
- (xiii)  $R^6$  is  $C_1$ - $C_4$ -alkyl;

R<sup>d</sup> is H or OH;

R<sup>e</sup> is CH<sub>3</sub>;
R<sup>f</sup> is OH; and
R<sup>j</sup> is H;